Approved for use through 10,31/99. OMB 0651-0031
Petent and Tradement Office; U.S. DEPARTMENT OF COMMERCE
spond to a collection of Information united & discharge a valid OMB control number.

| REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a) | | | | |
|--|---|---|--|--|
| RECEIVED SEP 1. 4 2000 File Information Unit | | Filed 57 Oct. 7, 1994 Thanks Paper No | | |
| Assistant Commissioner for Patents Washington, DC 20231 | | | | |
| I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above- Identified ABANDONED application, which is: (CHECK ONE) (A) referred to in United States Patent Number 5,998,13 column 6.7 (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No | | | | |
| | | | | |
| Signature Chris Riley Typed or printed name | | Oate OR PTO USE ONLY Approved by: [Initials] | | |
| | 1 | Unit: | | |



United States Patent [19]

Barr et al.

[11] Patent Number:

5,998,131

[45] Date of Patent:

Dec. 7, 1999

[54] SCREENING METHODS FOR THE IDENTIFICATION OF COMPOUNDS CAPABLE OF ABROGATING BAK-BHRF-1 PROTEIN INTERACTIONS

- [75] Inventors: Philip J. Barr, Berkeley; Michael C. Klefer, Clayton, both of Calif.
- [73] Assignee: LXR Biotechnology, Inc., Richmond, Calif.
- [21] Appl. No.: **08/944,530**
- [22] Filed: Oct. 7, 1997

Related U.S. Application Data

- [62] Continuation of application No. 08/426,529, Apr. 20, 1995, abandoned, which is a continuation-in-part of application No. 08/320,157, Oct. 7, 1994, which is a continuation-in-part of application No. 08/160,067, filed as application No. PCT/US94/13930, Nov. 30, 1994, abandoned.
- [51] Int. Cl.⁶ C12Q 1/70; A61K 39/245; A61K 39/23
- [52] U.S. Cl. 435/5; 424/230.1; 424/233.1

[56] References Cited

FOREIGN PATENT DOCUMENTS

| WO 93/04169 | 3/1993 | WIPO. |
|-------------|--------|-------|
| WO 94/00572 | 1/1994 | WIPO. |
| WO 95/00160 | 1/1995 | WIPO. |
| WO 95/00642 | 1/1995 | WIPO. |
| WO 95/05738 | 3/1995 | WIPO. |
| WO 95/05750 | 3/1995 | WIPO. |
| WO 95/15084 | 6/1995 | WIPO. |

OTHER PUBLICATIONS

Ameisen et al., "Cell dysfunction and depletion in AIDS: The programmed cell death hypothesis" *Immunol. Today* (1991) 12: 102-105.

Barr, "Expression of foreign genes in yeast" *Transgenesis* (1992) pp. 55-79.

Boise et al., "bcl-x, a bcl-2-related gene that functions as a dominant regulator of apoptotic cell death" Cell (1993) 74: 597-608.

Chen-Levy et al., "The bcl-2 candidate proto-oncogene product is a 24-kilodalton integral-membrane protein highly expressed in lymphoid cell lines and lymphomas carrying the t(14;18) translocation" Mol. Cell Biol. (1989) 9: 701-710.

Chittenden et al., "Unduction of apoptosis by the Bcl-2 homologue Bak" *Nature* (1995) 347: 733-736.

Clearly et al., "Cloning and structural analysis of cDNAs for bcl-2 and a hybrid bcl-2/immunoglobin transcript resulting from the t(14;18) translocation" *Cell* (1986) 47: 19-28.

Cohen et al., "Apoptosis and programmed cell death in immunity" Ann. Rev. Immunol. (1992) 10: 267-293.

Duke et al., "IL-2 addiction: Withdrawal of growth factor activates a suide program in dependent T Cells" Lymphokine Res. (1986) 5: 289-299.

Edgington, "Looking death in the eye: Apoptosis and cancer research" *Biotech.* (1993).

Farrow et al., "Cloning of a bcl-2 homologue by interaction with adenovirus E1B 19K" Nature (1995) 374: 731-733. Feinberg et al., "A technique for radiolabeling DNA restriction endonuclease to high specific actiity" Anal. Blochem (1984) 137: 266-267.

Gerchenson et al., "Apoptosis: A different type of cell death" FASEB J. (1992) 6: 2450–2455.

Hickish et al., "Ultrastructural localization of BHRF1: An Epstein-Barr virus gene product which has homology with bcl-2" Cancer Research (1994) 54: 2808–2811.

Hockenbery et al., "Bcl-2 functions in an antioxidant pathway to prevent apoptosis" Cell (1993) 75: 241-251.

(List continued on next page.)

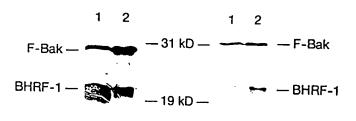
Primary Examiner—Laurie Scheiner Assistant Examiner—Jeffrey S. Parkin Attorney, Agent, or Firm—Sheridan Ross P.C.

71

The present invention provides methods for screening potential anti-viral therapeutic agents by monitoring their ability to disrupt the interaction between the BAK protein and a viral protein.

ABSTRACT

6 Claims, 8 Drawing Sheets



F-Bak/BHRF-1

F-Bak-2/BHRF-1

1) In vitro co-translated proteins

2) Proteins bound to anti-FLAG agarose

Approved for use through 1031/99, OMB 0551-0031 and Tradement Office; U.S. DEPARTMENT OF COMMERCE official of information unities a decisive a valid CMB control number.

Patent and Tradement Office; U.S. DEPARTMENT OF COMMERC

Patent and Tradement Office; U.S. DEPARTMENT OF COMMERC

Act of 199-, on persons are required to reasoned to a collection of information united it declays a veid OMB control number

| REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a) | | | | |
|---|---|--|--|--|
| RECEIVED SEP 4 4 2000 File Information Unit | In re Application of Application Number O8 160,067 Filed Nov. 30, 1994 Group Art Unit Examiner | | | |
| Assistant Commissioner for Patents Washington, DC 20231 | 7642 Paper No. 24 | | | |
| identified ABANDONED application, which is (A) referred to in United States Patent N | (a)(3)(iv) to the application file record of the above- tr (CHECK ONE) umber 5 98 3 column 62 pen to public inspection as set forth in 37 CFR 1.11, i.e., | | | |
| Application No paper number (C) an application that claims the benefit | t of the filing date of an application that is open to public | | | |
| (D) an application in which the applicant application to the public. | has filed an authorization to lay open the complete | | | |
| Please direct any correspondence concerning | ng this request to the following address: | | | |
| | | | | |
| Signature D | 9(14(00) Date | | | |
| Typed or printed name | FOR PTO USE ONLY Approved by: | | | |
| • · | Unit | | | |

Burcen Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

****SESSITENT Commissioner for Patents, Washington, DC 20231.



United States Patent [19]

Barr et al.

[11] Patent Number:

5,998,131

[45] Date of Patent:

Dec. 7, 1999

[54] SCREENING METHODS FOR THE IDENTIFICATION OF COMPOUNDS CAPABLE OF ABROGATING BAK-BHRF-1 PROTEIN INTERACTIONS

- [75] Inventors: Philip J. Barr, Berkeley; Michael C. Klefer, Clayton, both of Calif.
- [73] Assignee: LXR Biotechnology, Inc., Richmond, Calif.
- [21] Appl. No.: 08/944,530
- [22] Filed: Oct. 7, 1997

Related U.S. Application Data

- [62] Continuation of application No. 08/426,529, Apr. 20, 1995, abandoned, which is a continuation-in-part of application No. 08/320,157, Oct. 7, 1994, which is a continuation-in-part of application No. 08/160,067, filed as application No. PCT/US94/13930, Nov. 30, 1994, abandoned.
- [51] Int. Cl.⁶ C12Q 1/70; A61K 39/245; A61K 39/23

[56] References Cited

FOREIGN PATENT DOCUMENTS

| WO 93/04169 | 3/1993 | WIPO. |
|-------------|--------|-------|
| WO 94/00572 | 1/1994 | WIPO. |
| WO 95/00160 | 1/1995 | WIPO. |
| WO 95/00642 | 1/1995 | WIPO. |
| WO 95/05738 | 3/1995 | WIPO. |
| WO 95/05750 | 3/1995 | WIPO. |
| WO 95/15084 | 6/1995 | WIPO. |

OTHER PUBLICATIONS

Ameisen et al., "Cell dysfunction and depletion in AIDS: The programmed cell death hypothesis" *Immunol. Today* (1991) 12: 102–105.

Barr, "Expression of foreign genes in yeast" *Transgenesis* (1992) pp. 55-79.

Boise et al., "bcl-x, a bcl-2-related gene that functions as a dominant regulator of apoptotic cell death" Cell (1993) 74: 597-608.

Chen-Levy et al., "The bcl-2 candidate proto-oncogene product is a 24-kilodalton integral-membrane protein highly expressed in lymphoid cell lines and lymphomas carrying the t(14;18) translocation" Mol. Cell Biol. (1989) 9: 701-710.

Chittenden et al., "Unduction of apoptosis by the Bcl-2 homologue Bak" *Nature* (1995) 347: 733-736.

Clearly et al., "Cloning and structural analysis of cDNAs for bcl-2 and a hybrid bcl-2/immunoglobin transcript resulting from the t(14;18) translocation" Cell (1986) 47: 19-28.

Cohen et al., "Apoptosis and programmed cell death in immunity" Ann. Rev. Immunol. (1992) 10: 267-293.

Duke et al., "IL-2 addiction: Withdrawal of growth factor activates a suide program in dependent T Cells" Lymphokine Res. (1986) 5: 289-299.

Edgington, "Looking death in the eye: Apoptosis and cancer research" Biotech. (1993).

Farrow et al., "Cloning of a bcl-2 homologue by interaction with adenovirus E1B 19K" Nature (1995) 374: 731-733. Feinberg et al., "A technique for radiolabeling DNA restriction endonuclease to high specific actiity" Anal. Blochem (1984) 137: 266-267.

Gerchenson et al., "Apoptosis: A different type of cell death" FASEB J. (1992) 6: 2450-2455.

Hickish et al., "Ultrastructural localization of BHRF1: An Epstein-Barr virus gene product which has homology with bcl-2" Cancer Research (1994) 54: 2808-2811.

Hockenbery et al., "Bcl-2 functions in an antioxidant pathway to prevent apoptosis" Cell (1993) 75: 241-251.

(List continued on next page.)

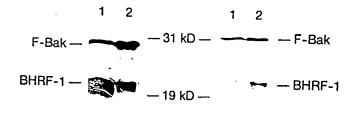
Primary Examiner—Laurie Scheiner Assistant Examiner—Jeffrey S. Parkin Attorney, Agent, or Firm—Sheridan Ross P.C.

[57]

ABSTRACT

The present invention provides methods for screening potential anti-viral therapeutic agents by monitoring their ability to disrupt the interaction between the BAK protein and a viral protein.

6 Claims, 8 Drawing Sheets



F-Bak/BHRF-1

F-Bak-2/BHRF-1

- 1) In vitro co-translated proteins
- 2) Proteins bound to anti-FLAG agarose